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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,414	08/19/2002	Jean-Marie Lehn	GMV-003.01	3270

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EXAMINER	
QAZI, SABIHA NAIM	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 01/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,414	LEHN, JEAN-MARIE	
	Examiner	Art Unit	
	Sabiha Qazi	1616	

-- Th MAILING DATE of this communication app ars on th cover she t with the correspondenc address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *44-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Non-Final Action on Merits

Acknowledgment is made of the response to the Election Requirement filed on Oct. 10, 2003, in paper no. 10. Applicants have elected Group I and requested to combine Group II for the examination. Applicants have elected the species wherein the cationic, lipophilic, water-soluble molecule is BGTC (See page 18 of Specification for definition) and the anionic ligand for a cellular receptor is inositol hexaphosphate.

Claims 1-49 are pending. Claims 1-43 are rejected; Claims 44-49 are withdrawn from consideration.

Presently claimed invention is drawn to a composition consisting essentially of a cationic, lipophilic, water-soluble molecule, and an anionic ligand for a cellular receptor and a compound represented by generalized structure 1 wherein C+ represents a lipophilic water-soluble molecule bearing at least one positive charge, and A- represents a ligand for a mammalian cellular receptor, wherein ligan bears at least one negative charge.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what is intended by "lipophilic water-soluble molecule" and "ligand for a cellular receptor" (Claims 1 and 11).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over the journal articles Pitard et al. The Pitard et al. reference teaches cationic cholesterol derivatives having guanidinium polar headgroups useful for gene transfection in vitro and in vivo. The reference teaches the use of bis(guanidinium)-tren-cholesterol (BGTC), either alone or as a liposomal formulation with the neutral phospholipd dioeoyl or as a liposomal formulation with the neutral phospholipid dioleoyl phosphatidylethanolamine (DOPE).

Instant claims differ from the reference in claiming a broader scope than the prior art. The prior art teaches BGTC whereas presently claimed invention is claiming any composition containing cationic, lipophilic, water-soluble molecule, and an anionic ligan for a cellular receptor and a compound represented by generalized structure 1 wherein C+ represents a

lipophilic water-soluble molecule bearing at least one positive charge, and A- represents a ligand for a mammalian cellular receptor, wherein ligand bears at least one negative charge.

It would have been obvious to one skilled in the art to prepare the presently claimed composition and the compound such as bis(guanidinium)-tren-cholesterol (BGTC) because the prior teaches the composition, compound, and its uses.

The search was limited to the elected species BGTC. The compounds of claim 11 encompass numerous numbers of compounds.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is 703-305-3910. The examiner can normally be reached on every business day.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

***

SABIHA QAZI, PH.D
PRIMARY EXAMINER

We claim:

1. A composition consisting essentially of a cationic, lipophilic, water-soluble molecule, and an anionic ligand for a cellular receptor.

2. The composition of claim 1, wherein the anionic ligand is a ligand for the allosteric site of hemoglobin.

3. The composition of claim 2, wherein the anionic ligand is an inositol polyphosphate.

4. The composition of claim 3, wherein the anionic ligand is inositol hexaphosphate.

5. The composition of claim 1, wherein the cationic, lipophilic, water-soluble molecule comprises a guanidinium moiety.

6. The composition of claim 5, wherein the cationic, lipophilic, water-soluble molecule is a sterol comprising at least one guanidinium moiety.

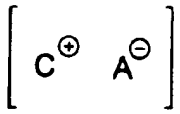
7. The composition of claim 5, wherein the cationic, lipophilic, water-soluble molecule is BGTC or BGSC.

8. The composition of claim 2, wherein the cationic, lipophilic, water-soluble molecule comprises a guanidinium moiety.

9. The composition of claim 3, wherein the cationic, lipophilic, water-soluble molecule is a sterol comprising at least one guanidinium moiety.

10. The composition of claim 4, wherein the cationic, lipophilic, water-soluble molecule is BGTC or BGSC.

11. A compound represented by generalized structure **1**:



1

wherein

C+ represents a lipophilic water-soluble molecule bearing at least one positive charge; and

A- represents a ligand for a mammalian cellular receptor, wherein said ligand bears at least one negative charge.

12. The compound of claim 11, wherein A- is a ligand for the allosteric site of hemoglobin.

13. The compound of claim 11, wherein C+ comprises at least one cationic functional group selected from the group consisting of guanidinium, imidazolium, 1,2-diammoniumethylene, 1,8-diammoniumnaphthyl, and 2,2'-bipyridinium.

14. The compound of claim 11, wherein C+ comprises at least one guanidinium moiety.

15. The compound of claim 11, wherein C+ comprises two guanidinium moieties.

16. The compound of claim 11, wherein C+ comprises at least one cationic functional group selected from the group consisting of guanidinium, imidazolium, 1,2-diammoniumethylene, 1,8-diammoniumnaphthyl, and 2,2'-bipyridinium; and A- is a ligand for the allosteric site of hemoglobin.

17. The compound of claim 11, wherein C+ comprises at least one guanidinium moiety; and A- is a ligand for the allosteric site of hemoglobin.

18. The compound of claim 11, wherein C+ comprises two guanidinium moieties; and A- is a ligand for the allosteric site of hemoglobin.

19. A compound consisting essentially of a lipophilic water-soluble molecule, wherein said lipophilic water-soluble molecule comprises at least one guanidine or guanidinium moiety; and a second molecule comprising at least one carboxylic acid, phosphoric acid, phosphonic acid, sulfuric acid, or sulfonic acid moiety.

20. The compound of claim 19, wherein said second molecule comprises at least one carboxylic acid or phosphoric acid moiety.

21. The compound of claim 19, wherein said second molecule is a phosphorylated inositol.

22. The compound of claim 19, wherein said second molecule is IHP.

23. The compound of claim 19, 20, or 21, wherein said second molecule is a ligand for the allosteric site of hemoglobin.

24. The compound of claim 19 or 20, wherein said lipophilic water-soluble molecule is a sterol.

25. The compound of claim 24, wherein said second molecule is a phosphorylated inositol.

26. The compound of claim 25, wherein said second molecule is IHP.

27. The compound of claim 24, wherein said second molecule is a ligand for the allosteric site of hemoglobin.

28. The compound of claim 25, wherein said second molecule is a ligand for the allosteric site of hemoglobin.

29. The compound of claim 24, wherein said sterol is cholesterol.

30. The compound of claim 25, wherein said sterol is cholesterol.

31. The compound of claim 26, wherein said sterol is cholesterol.

32. The compound of claim 29, wherein said second molecule is a ligand for the allosteric site of hemoglobin.

33. The compound of claim 30, wherein said second molecule is a ligand for the all steric site of hemoglobin.

34. The compound of claim 24, wherein said lipophilic water-soluble molecule is BGSC or BGTC.

35. The compound of claim 25, wherein said lipophilic water-soluble molecule is BGSC or BGTC.

36. The compound of claim 26, wherein said lipophilic water-soluble molecule is BGSC or BGTC.

37. The compound of claim 34, wherein said second molecule is a ligand for the allosteric site of hemoglobin.

38. The compound of claim 35, wherein said second molecule is a ligand for the allosteric site of hemoglobin.

39. The compound of claim 24, wherein said lipophilic water-soluble molecule is BGTC.

40. The compound of claim 25, wherein said lipophilic water-soluble molecule is BGTC.

41. The compound of claim 26, wherein said lipophilic water-soluble molecule is BGTC.

42. The compound of claim 39, wherein said second molecule is a ligand for the allosteric site of hemoglobin.

43. The compound of claim 40, wherein said second molecule is a ligand for the allosteric site of hemoglobin.

44. A method of enhancing oxygen delivery to a tissue or organ of a mammal, comprising the step of:

administering to said mammal a composition or compound according to claim 1 or 11.

45. A method of enhancing oxygen delivery to a tissue or organ of a mammal, comprising the step of:

administering to said mammal red blood cells previously treated with a composition or compound according to claim 1 or 11.

46. A method of treating a mammal afflicted with anemia, coronary infarction, pulmonary disease, congestive heart failure, myocardial infarction, stroke, peripheral vascular disease, intermittent claudication, circulatory shock, hemorrhagic shock, chronic hypoxia, respiratory alkalemia, metabolic alkalosis, sickle cell anemia, reduced lung capacity, gangrene, anaerobic infections, carbon monoxide poisoning, nitric oxide poisoning, or